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## Risks and benefits of UV radiation in older people - More of a friend than a foe?

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### Abstract

Incident ultraviolet radiation from sunlight varies in intensity and spectrum with season and latitude and has both deleterious and beneficial effects on health in older people. Sunlight is the major preventable risk factor for skin cancer. Non melanoma skin cancer is the commonest malignancy in a pale skinned older population, but the mortality is extremely low. Intermittent sun exposure is a risk factor for the more dangerous melanoma but chronic sun exposure and outdoor occupation may be protective. Public health advice has tended to concentrate on the dangers of sun exposure despite the absence of any data that increased sun exposure correlates with raised all-cause mortality.

Inadequate sun exposure carries its own risks, and the older population are particularly sun deprived as recorded by low serum Vitamin D levels and lack of outdoor activity. Sunlight has health benefits dependently and independently of vitamin D synthesis. Low serum vitamin D levels correlate with increased morbidity and mortality but the direction of association is not always clear. Vitamin D has a causal role in calcium and phosphate metabolism, in skeletal health and probably reduction of colorectal cancer. Evidence is weak for a role in cardiovascular health, but mobilisation of nitric oxide by UVA radiation from nitrate stores in skin, with consequent reduction in BP, may account for the observed reduction in cardiovascular disease and all-cause mortality with increased sun exposure. Advice on healthy sun exposure needs to be reconsidered, with reduction in all-cause mortality and morbidity as the primary end point.

### Key Words.

Sunlight; ultraviolet; vitamin D; nitric oxide; all-cause mortality; aging

### Introduction

Public health and advisory bodies currently advise that sun exposure (UV radiation) should be limited based on the associated adverse effects of which the most important is the development of skin cancer. [1]

The risks from excessive UV exposure are well established but benefits on several markers of health are also emerging, in addition to the main effect of cutaneous vitamin D synthesis. The association between vitamin D deficiency and a number of serious non-skeletal conditions is well described in the literature. It is unclear if vitamin D itself is responsible for all these relationships or is a surrogate marker of UV exposure, and other mechanisms are implicated. Biological effects of UV separate to Vitamin D photosynthesis are now being explored due to the apparent reduction in all cause mortality in populations with increased UV exposure.

The mortality and morbidity associated with hypertension and vascular disease in the older population far exceeds that of skin cancer and we will review the hypotheses pertaining to the role of UV in blood pressure modulation, cardiovascular disease and stroke.

There is significant variation in UV exposure dependent on latitude and environmental factors. Sun exposure advice should thus be tailored to local ambient conditions and geographical location.

The objectives of this review are to explore the evidence for the harm and benefit of UV exposure in the older adult population. Some of these benefits will be vitamin D related but we also explore the benefits that may be independent of vitamin D levels.

### Search Strategy

Pubmed, Medline, Embase, Cinahl and The Cochrane Databases were searched. No date or language restrictions were placed on the articles origins. Bibliographies from papers were also analysed for additional relevant publications.

All the articles were obtained and evaluated for relevance. Only those with the most relevance were used in this review. Key search words used in combination were: Ultraviolet Rays, Ultraviolet, UV, UV radiation, sunlight, sunlight exposure, old age, elderly, geriatric, aged, Benefit and harm. Finally, 50 articles were selected for inclusion.

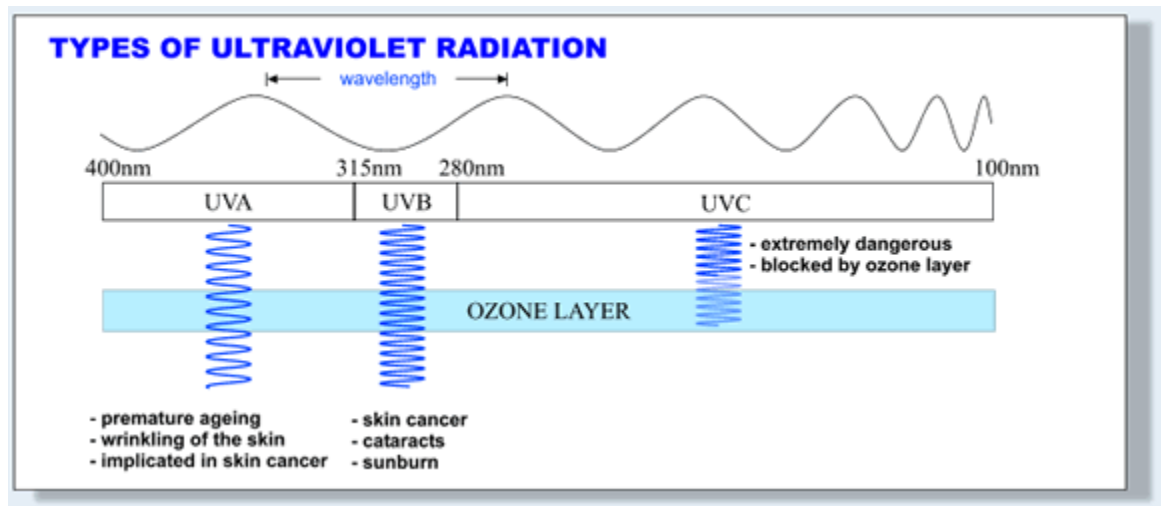
### Ultraviolet Radiation

Ultraviolet or solar radiation can be categorised according to its wavelength into UVA, UVB and UVC. Sunlight is predominantly comprised of UVA – 90% and UVB – 10%. Less than 2.5 % of the sun's radiation permeates through the earth's atmosphere and UVC is absorbed before reaching the Earth's surface [2]. Incident UV at the Earth's surface varies due to changes in atmospheric absorption, time of day, latitude, altitude, cloud cover and season.

Biological activity is wavelength dependant with UVA penetrating deeper into the dermis whilst UVB is largely absorbed within the epidermis. These wavelength differences determine the location and type of biological activity. Excessive exposure results in acute keratinocyte damage, apoptosis

and mutation to p53 suppressor genes. UVA damages DNA indirectly through free radical formation and oxidative injury, while UVB radiation causes direct DNA damage with signature mutations predisposing to skin cancers. Other biological effects of UV include photo ageing, inflammation and burning in addition to Vitamin D synthesis [3].

UVA – (315-400nm), UVB (280-315nm) and UVC (100-280nm)



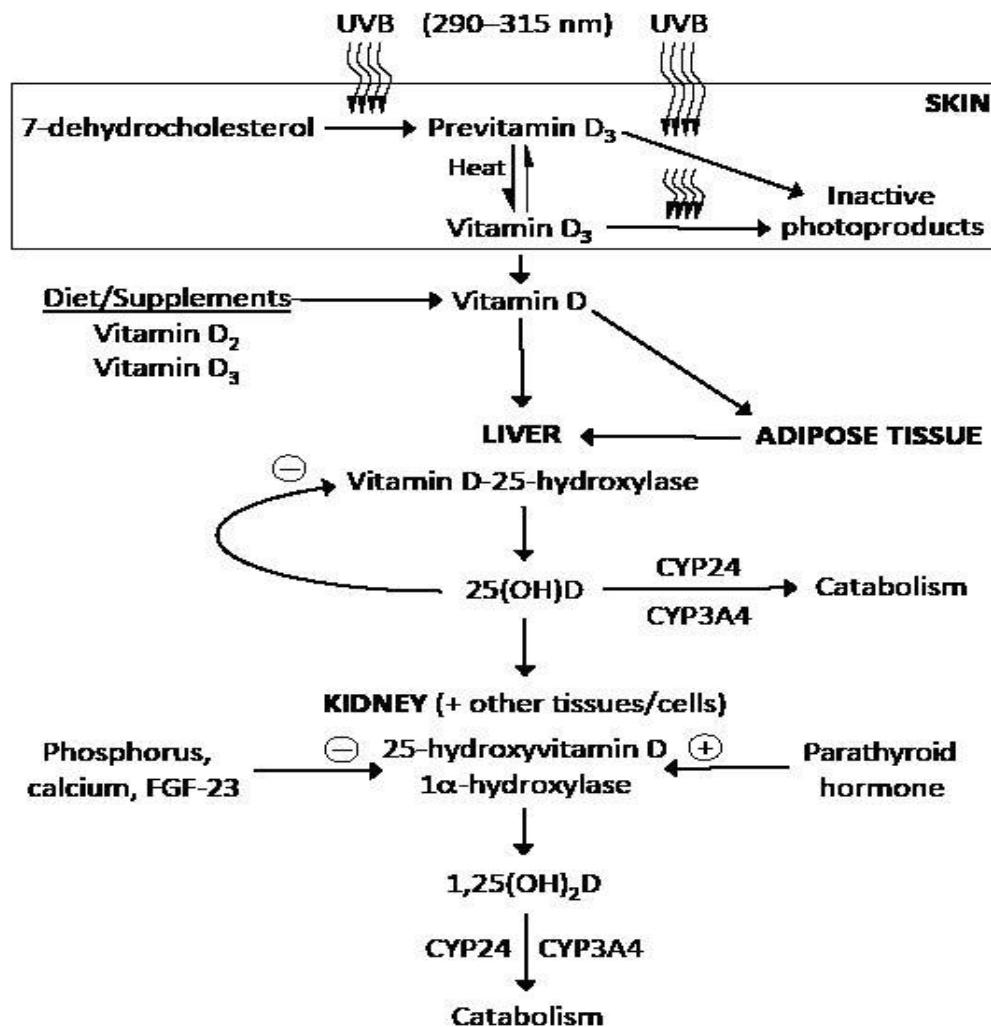
(Australian Government Radiation protection website  
<http://www.arpansa.gov.au/radiationprotection/basics/uvr.cfm>)

**Fig.1.** Types of ultraviolet radiation.

### **Risk versus Benefit**

Policies strictly limiting sun exposure are now being challenged in older adults [4]. 20% of the UK population aged > 65yrs cannot recall the last episode of any form of outdoor exercise [5] and vitamin D deficiency in the older population is widespread [6].

## Vitamin D



**Fig. 2.** (Diagram from Factors influencing vitamin D status. [7])

The key role of Vitamin D is to optimise calcium and phosphate absorption from the gut, but it probably has beneficial health effects beyond this.

Once absorbed in the gut or produced in the skin, vitamin D is hydroxylated to 25OHD by the liver. Serum levels of 25OHD are used as indicators of Vitamin D status. 1, 25 OHD – (calcitriol) - the biologically active form is produced in the kidney. Renal production of calcitriol is regulated by calcium via PTH.

There is a general consensus that a level of 25(OH) D  $<25$  nmol/l (or 10 ng/ml) is deficient but there is less agreement with regard to what the optimal level of circulating 25(OH) D should be. Despite this, specific serum levels have been recommended with respect to bone health and also suggested to reduce the risk of non skeletal illnesses [8].

Skin production of vitamin D is governed and influenced by a number of racial and environmental factors [9]. Vitamin D deficiency is linked to an increasing number of pathological processes although controversy regarding the causality in these associations continues particularly as Vitamin D “deficiency” is very prevalent.

Recommendations regarding the optimal duration of sun / UVB exposure to enable “adequate” vitamin D synthesis are complicated by variations in UV intensity relating to latitude, time of day, season, cloud cover, skin pigmentation and clothing [10]. Pigmented skin requires longer UV exposure to synthesise vitamin D due to UVB absorption by melanin

Attempts have been made to take into account environmental and racial differences when recommending sun exposure time [11]. Prolonged sun exposure does not cause Vitamin D levels to continue to rise indefinitely. With age, human skin atrophies and there is a resultant reduction in dermal synthesis of vitamin D after exposure to UVB [12]. This reduction in vitamin D photosynthesis is compounded by older adults also spending less time in sunlight due to attitudes, opportunity and frailty [13].

Lower serum levels of Vitamin D are unsurprisingly linked with multimorbidity and ill health but the direction of the association is unclear. A large number of intervention studies with oral Vitamin D supplementation have been performed to resolve this question. These have recently been meta-analysed, although different trial designs of the underlying studies (dose of vitamin D; concomitant administration or not of calcium; entry criteria; duration of intervention) have meant that even these large meta-analyses have not been consistent in their findings

A meta-analysis of randomised controlled trials by Zheng et al suggested a reduction in all-cause mortality with Vitamin D supplementation [14] but only after long term (greater than 3 years) supplementation.

A separate meta-analysis concluded that Vitamin D3 supplementation appeared to reduce mortality only in older female subjects living either independently or in institutional care [15].

Analysis of observational studies and intervention studies of Vitamin D supplementation did not demonstrate a reduction in malignancy with supplementation and it was thus postulated that low vitamin D levels may merely be a marker of poor health [16].

A different approach to the question of the effects of Vitamin D on all cause mortality is to use the natural experiment of Mendelian randomisation. Several genetic polymorphisms carried in the population lead to reduced endogenous production of active 1, 25 OH vitamin D. A study of almost 100,000 Danes showed that carrying the ‘low vitamin D’ genotype conferred an increased risk of cancer and all cause death, but had no effect on cardiovascular mortality [17]

### Bone / muscle function / Falls

Vitamin D deficiency is associated with muscle weakness and this compounded by bone density loss leads to the potential for increased falls and fracture risk in older adults [5]. It is suggested that reduced sunlight exposure and presumably Vitamin D levels are associated with cartilage loss and Osteoarthritis [18]. Sarcopenia is also associated with Vitamin D insufficiency [19].

Environmental and geographical effects on UV strength influencing Vitamin D synthesis are implicated in the bone health of the aged. Incident UV at the earth's surface is reduced at higher latitudes. Hip fracture incidence correlates directly with latitude [20].

### Immune System and Insulin Sensitivity

Calcitriol 1, 25 OH D (Vit D 3) is involved in immune system modulation. Numerous autoimmune diseases are associated with vitamin D deficiency including asthma; inflammatory bowel disease, MS and Rheumatoid Arthritis. Some of the effects on immunomodulation are felt to be separate to the effects of UVR [21]. Both UVA and UVB have direct immunosuppressive effects by up regulating TNF alpha, IL-10 and T regulatory cells to offer protection from autoimmune conditions [22].

Vitamin D has been implicated in insulin sensitivity with vitamin D levels being inversely related to insulin resistance in populations including older adults [23]. UV exposure may also reduce obesity and metabolic syndrome independently of Vitamin D [24].

### Cancer

Observational and epidemiological studies have shown associations between low vitamin D levels and certain cancers. These observations are not conclusive of causality and remain controversial [25]. Results have been largely inconsistent with the exception of the development and prognosis of colorectal cancer [26].

Whilst low levels of vitamin D are associated with higher rates of malignancy, higher levels do not appear to be protective, again with the exception of colon cancer [16]. Overall, supplementation does not appear to be preventative in a recent Cochrane systematic review [27].

As vitamin D levels are influenced by a number of variables, UVR has been studied to independently assess its effect. A prospective study including people aged up to 71 years demonstrated that, excluding melanoma, UVR exposure was inversely associated with total cancer risk [28].

A case - control study of the whole population of Denmark over the age of 40 demonstrated the unexpected finding of a reduction in both all - cause mortality and myocardial infarction in those with non-melanoma skin cancer [29], a marker for chronic sun exposure.

Similarly, a large prospective cohort study showed that avoidance of sun in Swedish women was associated with a significant increase in all-cause mortality with a 3% population attributable risk of all-cause mortality due to inadequate sun exposure [30].

## Skin Cancers

The global incidence of skin cancer continues to rise. The commonest cutaneous cancers can be subdivided into Malignant Melanoma (MM) and Non Melanoma Skin Cancer (NMSC).

### Malignant Melanoma (MM)

For the purposes of this review we will refer to cutaneous MM – CMM. All subtypes occur in the elderly but superficial spreading MM is the commonest form diagnosed in older adults. Lentigo maligna melanoma (LMM) is similar to superficial spreading melanoma and is particularly a disease of the elderly. It is associated with chronic sun exposure and tends to develop on classical sites of sun exposure and damage e.g. head, ears, upper torso and arms.

The major MM risk factors are: Caucasian race; type I and II skin (i.e. more likely to burn in the sun); multiple episodes of severe sunburn particularly in childhood; intermittent sunlight exposure or tanning bed use, and the presence of dysplastic naevi.

In those older than 60 years, chronic sun exposure, smoking, large number of melanocytic naevi and a history of prior neoplasia including NMSC are risk factors for CMM as is tumour susceptibility and intense sun exposure [31].

The relationship between sun exposure and melanoma is not straight-forward however with increased sun exposure being associated with melanoma survival [32] and chronic occupational sun exposure correlating inversely with incident melanoma [33].

### NMSC

The two commonest forms of non melanoma skin cancer (NMSC) are basal cell carcinomas and squamous cell carcinomas. Sunlight exposure is the major preventable risk factor for these. NMSC are very common. The annual incidence rate is around 260,000 cases [34] in the UK although as many- maybe most- go unreported, this is probably an underestimate. By comparison, there were 331,487 new cases of all other cancer types combined in the UK in 2011 (CRUK figures). Although extremely common, deaths from NMSC are rare. There were 638 such deaths in 2012, mostly due to SCC (CRUK figures)

### Squamous Cell Carcinoma (SCC)



SCC is commoner in men with 60 years being the average age at onset. The risk factors are largely similar to BCC but they tend to occur later in life. SCC is more associated with chronic sun exposure than the intermittent exposure risk seen with BCC and melanoma.

### Basal cell carcinoma (BCC)

The most common cancer diagnosed in Britain and the USA and predominantly occurs in older Caucasians with > 80% occurring on the head and neck. Not all, however, occur on sun exposed skin.

BCC is associated with higher cumulative sun exposure and intermittent exposure and is similar in that regard to MM.

Older adults may present later due to decreased awareness of lesions or physical limitations affecting their ability to check skin for suspicious lesions.

### Community Dwelling and institutionalised Older Adults Evidence

Older adults in care home facilities have significantly reduced time outdoors due to a constellation of frailty, reduced opportunity, personal disinclination and weather conditions [35].

Institutionalised older adults also have a high incidence of vitamin D deficiency. Researchers have previously explored providing UV light artificially indoors, the aim being to improve vitamin D levels as an alternative to oral supplementation and the potential side effects of medication and polypharmacy.

Some studies have focused on nursing home residents who specifically have very limited outdoor exposure, if any at all. Artificial UV has been demonstrated to reduce the biomarkers of excessive bone turnover associated with vitamin D deficiency and suppressing secondary hyperparathyroidism [36].

The Concord study from Australia analysed community dwelling older men and found that vitamin D deficiency was prevalent at 43-54% depending on the season despite them residing in a sunny geographical location. Lifestyle factors were highly influential [31].check

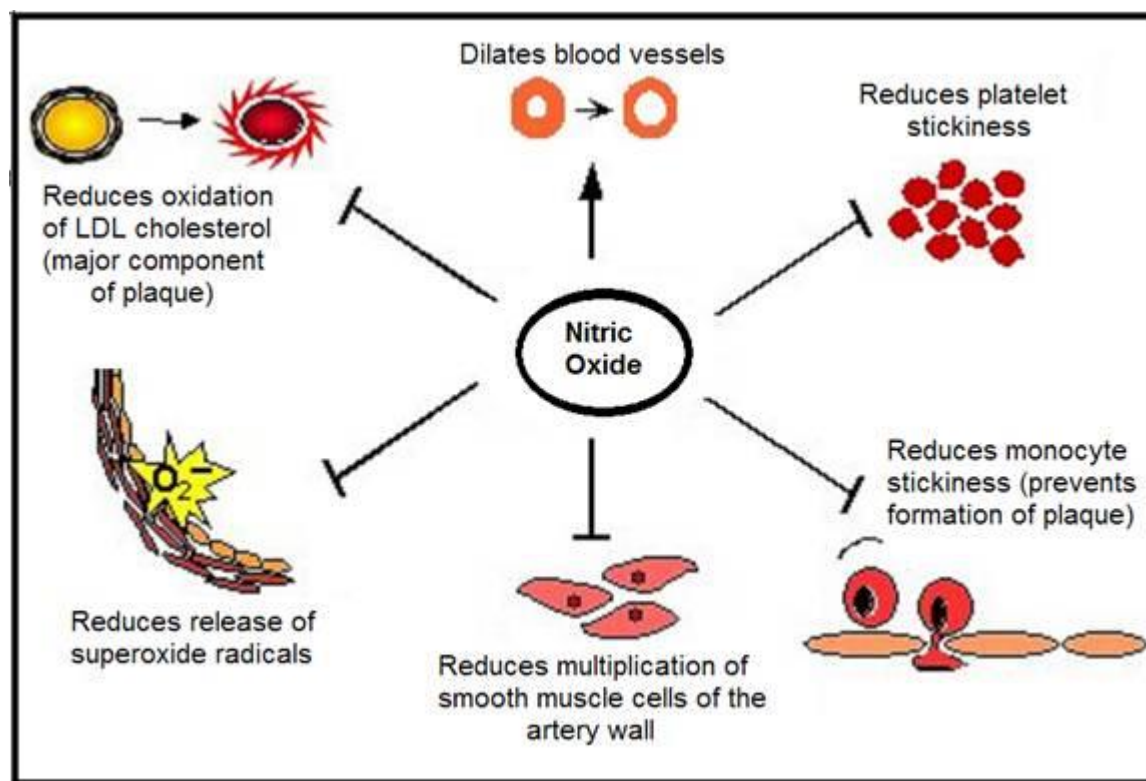
Heat related illnesses are more likely in older adults exposed to excessive warm sunlight and elevated temperature due to the combination of multimorbidity, impaired auto regulatory mechanisms, behaviours and multiple medications which may impair their homeostatic mechanisms [37].

### Phototherapy – therapeutic benefits of UV - Skin benefits

Phototherapy is widely used in dermatology as an effective treatment for a number of dermatoses, including psoriasis, atopic dermatitis, localised scleroderma and vitiligo. While treatment with early generation PUVA (psoralen and UVA) carried an increased risk of skin cancer development, this does not appear to be a complication of more modern narrow band UVB treatment [38].

### Vascular Disease and UV Exposure

Measured vitamin D levels show a strong inverse association with incident cardiovascular disease and death [8] . However, vitamin D supplementation has been shown in multiple independent randomised trials to have no effect on the development of cardiovascular disease (reviewed by Autier [16] and Judd [39] and individuals with genetically lower vitamin D synthesis have no difference in cardiovascular disease to the wild type population [17]. Vitamin D as well as having biological effects, also acts as a biomarker for sun exposure, and sun exposure may independently have benefits on cardiovascular health [40].



**Fig.3.** Some of the physiological effects of nitric oxide

A likely mechanism by which sunlight may benefit cardiovascular health in particular is via nitric oxide release. Nitric oxide has many biological effects as a signalling molecule within the body. One effect is the relaxation of vascular smooth muscle and resultant blood pressure reduction [41].

UVA mobilises nitric oxide and active metabolites from stores within the skin to the systemic circulation where it lowers blood pressure. This effect has been shown to be independent of temperature and Vitamin D synthesis and may help explain the variation in vascular morbidity observed with latitude when adjusting for other confounding variables [42][43].

Enzymatic production of NO is reduced with ageing, as is endothelial function and this decline may be implicated in the increased incidence of hypertension and vascular disease associated with the ageing process. Strategies to address this may have substantial effects on associated diseases rife within the older population [44].

Stroke incidence is affected by sunlight exposure. Analysis of The REGARDS study suggests an effect of sunlight on stroke incidence. An association between increased stroke incidence and lower levels of sun exposure was identified [45].

This Seasonal variation in stroke incidence is particularly observed in those over 65yrs [46].

### Mood and Cognition

Keratinocytes produce opioid B-endorphin following UV exposure and this effect may be implicated in tanning 'addiction'. Sun exposure is associated with improved mood and increased energy levels [47]. Melatonin and serotonin regulation is influenced by sunlight and improvement in cognition is seen with increased sun exposure particularly in depressed individuals [48].

### Cosmetic

Photoageing of the skin includes wrinkling, pigmentation, telangiectasias and atrophy in addition to skin cancers. Older women are aware and concerned by the cosmetic effects of photoageing. They demonstrate balanced attitudes to perceived benefits of sun exposure against the potential risks [49].

### Cataracts and Macular Degeneration

Ultraviolet radiation is absorbed by the lens and is implicated in cataract development with UV exposure implicated in cortical cataracts in particular. A U-shaped association between early AMD and UVR exposure has been observed with an increased risk for low- and high-exposures [50].

### Conclusions

Further scrutiny and study are required regarding the potential benefits of UV radiation based on plausible mechanisms of benefit in addition to harm particularly in the elderly.

There is a need to review recommendations of sun avoidance as this may be to the detriment not only of vitamin D synthesis but also of more relevant health endpoints such as reduced all cause mortality, hip fractures, blood pressure and vascular events.

Older adults should adopt a balanced approach to sun exposure. Behavioural recommendations should be tailored to race/ skin type and geographical location given the variation in UVR with latitude. Public health recommendations may evolve to warn of the dangers of inadequate or insufficient UV exposure in addition to excessive exposure.

Emerging evidence and theories may prompt revision of previously held beliefs and public health advice concerning sun exposure and behaviours of all ages including older adults.

Given the high prevalence of hypertension and vascular disease in the older population, dedicated research into the effects of UVR and NO interplay in vascular pathological processes in this group is of Public Health relevance.

Sun exposure can have harmful effects. Sun avoidance, common in the elderly, is undoubtedly harmful. A balance must be met. Dedicated research in the elderly is required.

#### **Competing interests**

None declared.

## **References**

- [1] Armstrong BK, Kricker A. The epidemiology of UV induced skin cancer. *J Photochem Photobiol Biol* 2001;63:8–18. doi:S1011134401001981 [pii].
- [2] D’Orazio J, Jarrett S, Amaro-Ortiz A, Scott T. UV Radiation and the Skin. *Int J Mol Sci* 2013;14:12222–48. doi:10.3390/ijms140612222 [doi].
- [3] Sarasin A. The molecular pathways of ultraviolet-induced carcinogenesis. *Mutat Res* 1999;428:5–10. doi:S1383-5742(99)00025-3 [pii].
- [4] Glossmann H. Vitamin D, UV, and skin cancer in the elderly: to expose or not to expose? *Gerontology* 2011;57:350–3. doi:10.1159/000322521.
- [5] Bischoff-Ferrari HA, Dietrich T, Orav EJ, Hu FB, Zhang Y, Karlson EW, et al. Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged > or =60 y. *Am J Clin Nutr* 2004;80:752–8. doi:80/3/752 [pii].
- [6] Sherman FT. Vitamin D deficiency is rampant in older adults. *Geriatrics* 2008;63:9–11.
- [7] Tsiaras WG, Weinstock MA. Factors influencing vitamin D status. *Acta Derm Venereol* 2011;91:115–24. doi:10.2340/00015555-0980 [doi].
- [8] Anderson JL, May HT, Horne BD, Bair TL, Hall NL, Carlquist JF, et al. Relation of vitamin D deficiency to cardiovascular risk factors, disease status, and incident events in a general healthcare population. *Am J Cardiol* 2010;106:963–8. doi:10.1016/j.amjcard.2010.05.027 [doi].
- [9] Dawson-Hughes B. Racial/ethnic considerations in making recommendations for vitamin D for adult and elderly men and women. *Am J Clin Nutr* 2004;80:1763S – 6S. doi:80/6/1763S [pii].
- [10] Mason RS, Sequeira VB, Gordon-Thomson C. Vitamin D: the light side of sunshine. *Eur J Clin Nutr* 2011;65:986–93. doi:10.1038/ejcn.2011.105 [doi].
- [11] Webb AR, Engelsen O. Calculated ultraviolet exposure levels for a healthy vitamin D status. *Photochem Photobiol* 2006;82:1697–703. doi:2005-09-01-RA-670 [pii].
- [12] Gilchrest BA, Stoff JS, Soter NA. Chronologic aging alters the response to ultraviolet-induced inflammation in human skin. *J Invest Dermatol* 1982;79:11–5.
- [13] Durvasula S, Sambrook PN, Cameron ID. Factors influencing adherence with therapeutic sunlight exposure in older people in intermediate care facilities. *Arch Gerontol Geriatr* 2012;54:e234–41. doi:http://dx.doi.org/10.1016/j.archger.2011.08.009.

- [14] Zheng Y, Zhu J, Zhou M, Cui L, Yao W, Liu Y. Meta-analysis of long-term vitamin D supplementation on overall mortality. *PLoS One* 2013;8:e82109. doi:10.1371/journal.pone.0082109 [doi].
- [15] Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, et al. Vitamin D supplementation for prevention of mortality in adults. *Cochrane Database Syst Rev* 2014;1:CD007470. doi:10.1002/14651858.CD007470.pub3 [doi].
- [16] Autier P, Boniol M, Pizot C, Mullie P. Vitamin D status and ill health: a systematic review. *lancetDiabetes Endocrinol* 2014;2:76–89. doi:10.1016/S2213-8587(13)70165-7 [doi].
- [17] Afzal S, Brondum-Jacobsen P, Bojesen SE, Nordestgaard BG. Genetically low vitamin D concentrations and increased mortality: mendelian randomisation analysis in three large cohorts. *BMJ* 2014;349:g6330. doi:10.1136/bmj.g6330 [doi].
- [18] Ding C, Cicuttini F, Parameswaran V, Burgess J, Quinn S, Jones G. Serum levels of vitamin D, sunlight exposure, and knee cartilage loss in older adults: the Tasmanian older adult cohort study. *Arthritis Rheum* 2009;60:1381–9. doi:10.1002/art.24486 [doi].
- [19] Scott D, Blizzard L, Fell J, Ding C, Winzenberg T, Jones G. A prospective study of the associations between 25-hydroxy-vitamin D, sarcopenia progression and physical activity in older adults. *Clin Endocrinol (Oxf)* 2010;73:581–7. doi:10.1111/j.1365-2265.2010.03858.x [doi].
- [20] Johnell O, Borgstrom F, Jonsson B, Kanis J. Latitude, socioeconomic prosperity, mobile phones and hip fracture risk. *Osteoporos Int* 2007;18:333–7. doi:10.1007/s00198-006-0245-4 [doi].
- [21] Hart PH, Gorman S, Finlay-Jones JJ. Modulation of the immune system by UV radiation: more than just the effects of vitamin D? *Nat Rev* 2011;11:584–96. doi:10.1038/nri3045 [doi].
- [22] Need AG, O’Loughlin PD, Horowitz M, Nordin BE. Relationship between fasting serum glucose, age, body mass index and serum 25 hydroxyvitamin D in postmenopausal women. *Clin Endocrinol (Oxf)* 2005;62:738–41. doi:CEN2288 [pii].
- [23] Badawi A, Sayegh S, Sadoun E, Al-Thani M, Arora P, Haddad PS. Relationship between insulin resistance and plasma vitamin D in adults. *Diabetes Metab Syndr Obes* 2014;7:297–303. doi:10.2147/DMSO.S60569 [doi].
- [24] Geldenhuys S, Hart PH, Endersby R, Jacoby P, Feelisch M, Weller RB, et al. Ultraviolet radiation suppresses obesity and symptoms of metabolic syndrome independently of vitamin D in mice fed a high-fat diet. *Diabetes* 2014;63:3759–69. doi:10.2337/db13-1675 [doi].
- [25] Grant WB. Relation between prediagnostic serum 25-hydroxyvitamin D level and incidence of breast, colorectal, and other cancers. *J Photochem Photobiol Biol* 2010;101:130–6. doi:10.1016/j.jphotobiol.2010.04.008 [doi].
- [26] Klampfer L. Vitamin D and colon cancer. *World J Gastrointest Oncol* 2014;6:430–7. doi:10.4251/wjgo.v6.i11.430 [doi].
- [27] Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Krstic G, Wetterslev J, et al. Vitamin D supplementation for prevention of cancer in adults. *Cochrane Database Syst Rev* 2014;6:CD007469. doi:10.1002/14651858.CD007469.pub2 [doi].

- [28] Lin SW, Wheeler DC, Park Y, Spriggs M, Hollenbeck AR, Freedman DM, et al. Prospective study of ultraviolet radiation exposure and mortality risk in the United States. *Am J Epidemiol* 2013;178:521–33. doi:10.1093/aje/kws589 [doi].
- [29] Brondum-Jacobsen P, Nordestgaard BG, Nielsen SF, Benn M. Skin cancer as a marker of sun exposure associates with myocardial infarction, hip fracture and death from any cause. *Int J Epidemiol* 2013;42:1486–96. doi:10.1093/ije/dyt168 [doi].
- [30] Lindqvist PG, Epstein E, Landin-Olsson M, Ingvar C, Nielsen K, Stenbeck M, et al. Avoidance of sun exposure is a risk factor for all-cause mortality: results from the Melanoma in Southern Sweden cohort. *J Intern Med* 2014;276:77–86. doi:10.1111/joim.12251 [doi].
- [31] Nagore E, Hueso L, Botella-Estrada R, Alfaro-Rubio A, Serna I, Guallar J, et al. Smoking, sun exposure, number of nevi and previous neoplasias are risk factors for melanoma in older patients (60 years and over). *J Eur Acad Dermatol Venereol* 2010;24:50–7. doi:10.1111/j.1468-3083.2009.03353.x [doi].
- [32] Berwick M, Armstrong BK, Ben-Porat L, Fine J, Krickler A, Eberle C, et al. Sun exposure and mortality from melanoma. *J Natl Cancer Inst* 2005;97:195–9. doi:97/3/195 [pii].
- [33] Gandini S, Sera F, Cattaruzza MS, Pasquini P, Picconi O, Boyle P, et al. Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure. *Eur J Cancer* 2005;41:45–60. doi:S0959-8049(04)00833-0 [pii].
- [34] Leigh IM. Progress in skin cancer: the U.K. experience. *Br J Dermatol* 2014;171:443–5. doi:10.1111/bjd.13258 [doi].
- [35] Durvasula S, Kok C, Sambrook PN, Cumming RG, Lord SR, March LM, et al. Sunlight and health: Attitudes of older people living in intermediate care facilities in southern Australia. *Arch Gerontol Geriatr* 2010;51:e94–9. doi:http://dx.doi.org/10.1016/j.archger.2010.01.008.
- [36] Chel VGM, Ooms ME, Pavel S, De Gruijl F, Brand A, Lips P. Prevention and treatment of vitamin D deficiency in Dutch psychogeriatric nursing home residents by weekly half-body UVB exposure after showering: a pilot study. *Age Ageing* 2011;40:211–4.
- [37] Hansen A, Bi P, Nitschke M, Pisaniello D, Newbury J, Kitson A. Older persons and heat-susceptibility: the role of health promotion in a changing climate. *Health Promot J Austr* 2011;22 Spec No:S17–20.
- [38] Paul C, Gallini A, Archier E, Castela E, Devaux S, Aractingi S, et al. Evidence-based recommendations on topical treatment and phototherapy of psoriasis: systematic review and expert opinion of a panel of dermatologists. *J Eur Acad Dermatol Venereol* 2012;26 Suppl 3:1–10. doi:10.1111/j.1468-3083.2012.04518.x [doi].
- [39] Judd SE, Tangpricha V. Vitamin D deficiency and risk for cardiovascular disease. *Am J Med Sci* 2009;338:40–4. doi:10.1097/MAJ.0b013e3181aaee91 [doi].
- [40] Feelisch M, Gorman S, Weller RB. Vitamin D status and ill health. *lancetDiabetes Endocrinol* 2014;2:e8–8587(14)70043–9. doi:10.1016/S2213-8587(14)70043-9 [doi].
- [41] Ignarro LJ, Buga GM, Wood KS, Byrns RE, Chaudhuri G. Endothelium-derived relaxing factor produced and released from artery and vein is nitric oxide. *Proc Natl Acad Sci U S A* 1987;84:9265–9.

- [42] Oplander C, Volkmar CM, Paunel-Gorgulu A, van Faassen EE, Heiss C, Kelm M, et al. Whole body UVA irradiation lowers systemic blood pressure by release of nitric oxide from intracutaneous photolabile nitric oxide derivatives. *Circ Res* 2009;105:1031–40. doi:10.1161/CIRCRESAHA.109.207019 [doi].
- [43] Liu D, Fernandez BO, Hamilton A, Lang NN, Gallagher JM, Newby DE, et al. UVA irradiation of human skin vasodilates arterial vasculature and lowers blood pressure independently of nitric oxide synthase. *J Invest Dermatol* 2014;134:1839–46. doi:10.1038/jid.2014.27 [doi].
- [44] Torregrossa AC, Aranke M, Bryan NS. Nitric oxide and geriatrics: Implications in diagnostics and treatment of the elderly. *J Geriatr Cardiol* 2011;8:230–42. doi:10.3724/SP.J.1263.2011.00230 [doi].
- [45] Kent ST, McClure LA, Judd SE, Howard VJ, Crosson WL, Al-Hamdan MZ, et al. Short- and long-term sunlight radiation and stroke incidence. *Ann Neurol* 2013;73:32–7. doi:10.1002/ana.23737.
- [46] Wang Y, Levi CR, Attia JR, D’Este CA, Spratt N, Fisher J. Seasonal variation in stroke in the Hunter Region, Australia: a 5-year hospital-based study, 1995–2000. *Stroke* 2003;34:1144–50. doi:10.1161/01.STR.0000067703.71251.B6 [doi].
- [47] Levins PC, Carr DB, Fisher JE, Momtaz K, Parrish JA. Plasma beta-endorphin and beta-lipoprotein response to ultraviolet radiation. *Lancet* 1983;2:166.
- [48] Kent ST, McClure LA, Crosson WL, Arnett DK, Wadley VG, Sathakumar N. Effect of sunlight exposure on cognitive function among depressed and non-depressed participants: a REGARDS cross-sectional study. *Environ Health* 2009;8:34. doi:10.1186/1476-069X-8-34 [doi].
- [49] Hurd Clarke L, Korotchenko A. Older women and suntanning: the negotiation of health and appearance risks. *Sociol Health Illn* 2009;31:748–61. doi:10.1111/j.1467-9566.2009.01175.x [doi].
- [50] Delcourt C, Cougnard-Gregoire A, Boniol M, Carriere I, Dore JF, Delyfer MN, et al. Lifetime exposure to ambient ultraviolet radiation and the risk for cataract extraction and age-related macular degeneration: the Alienor Study. *Invest Ophthalmol Vis Sci* 2014;55:7619–27. doi:10.1167/iovs.14-14471 [doi].